

### **Remarks**

Entry of this amendment and reconsideration of the subject application in view thereof are respectfully requested.

#### ***I. Claim Status***

Claims 1-44 are pending in the application. Claims 1, 21 and 24 have been amended to clarify the invention. New claim 45 has been presented. No new matter is added.

#### ***II. Response to Rejection Under 35 U.S.C. § 112***

Claims 1, 4 and 9 stood rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner has asserted that claim 1 is rendered indefinite for reciting “a heterocyclic group selected from phenyl, benzyl, etc.” Applicants believe that entry of the amendment to claim 1 overcomes the rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

#### ***III. Response to Rejections Under 35 U.S.C. §102***

##### ***Goodsall***

Claim 1 stood rejected under 35 U.S.C. §102(b) as being anticipated by Goodsall et al., U.S. Patent No. 6,113,965 (“Goodsall”). Applicants respectfully traverse this rejection.

Claim 1 is directed to a benzotropolone derivative represented by a formula having specific R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> groups.

Goodsall relates to the production of theaflavins and provides structure of various theaflavins (i.e., theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3, 3'-digallate) in Figure 2. The theaflavins taught by Goodsall do not have the same structural formula as the benzotropolone derivative set forth in Claim 1. For example, the R<sub>1</sub> and R<sub>2</sub> in the theaflavins are benzopyranyl groups. In contrast, R<sub>1</sub> in the benzotropolone derivative recited in

claim 1 is not benzopyranyl group. Goodsall does not teach or disclose a benzotropolone derivative wherein R<sub>1</sub> is not benzopyranyl group.

Anticipation requires that each and every limitation of a claim be found either expressly or inherently in a single prior art reference. *Bristol-Myers Squibb v. Ben Venue*, 246 F.3d 1368, 1374 (Fed. Cir. 2001). Absence from the reference of any claimed element negates anticipation. *Kloster Speedsteel AB v. Crucible, Inc.*, 230 USPQ 81 (Fed. Cir. 1986).

As such, given the strict identity required of the test for novelty, the Examiner has not established a *prima facie* case of anticipation in support of the rejection of claim 1 based on the Goodsall reference. Therefore, contrary to the Examiner's assertion, Goodsall does not anticipate claim 1 as it does not teach or disclose each and every limitation set forth in this claim. Accordingly, reconsideration and withdrawal of the rejection based on Goodsall under 35 U.S.C. §102 (b) are respectfully requested.

### ***Sang***

Claim 1 stood rejected under 35 U.S.C. §102 (a) as being anticipated by Sang et al., 2002, Tetrahedron Letters, Vol. 43: 7129-7133 ("Sang"). Applicants respectfully traverse this rejection.

Compound 3 of Sang is theaflavin-3-gallate wherein R<sub>1</sub> and R<sub>2</sub> are benzopyranyl groups. Compound 4 of Sang is theadibenzotropolone wherein R<sub>1</sub> and R<sub>2</sub> are benzopyranyl groups. In contrast, R<sub>1</sub> in the benzotropolone derivative recited in claim 1 is not benzopyranyl group. Accordingly, reconsideration and withdrawal of the rejection of claim 1 based on Sang are respectfully requested.

Claims 27 and 28 also stood rejected under 35 U.S.C. §102 (a) as being anticipated by Sang.

Claims 27 and 28 are directed to a method for synthesizing a benzotropolone derivative by reacting molecules in the presence of a peroxidase and H<sub>2</sub>O<sub>2</sub>.

In response, Applicants respectfully submit that in light of the Rule 132 declaration submitted herewith, the Sang reference has been removed as a prior art reference.

Reconsideration and withdrawal of this rejection based on Sang are respectfully requested.

***Lewis***

Claim 1 stood rejected under 35 U.S.C. §102 (b) as being anticipated by Lewis et al., 1998, *Phytochemistry*, Vol. 49: 2511-2519 (“Lewis”). Applicants respectfully traverse this rejection.

Lewis discloses the structure of theaflavate B. The R<sub>1</sub> and R<sub>2</sub> in this compound are benzopyranyl groups. In contrast, R<sub>1</sub> in the benzotropolone derivative recited in claim 1 is not benzopyranyl group. Lewis does not teach or disclose a benzotropolone derivative wherein R<sub>1</sub> is not benzopyranyl group. Therefore, contrary to the Examiner's assertion, Lewis does not anticipate claim 1 as it does not teach or disclose each and every limitation set forth in this claim. Accordingly, reconsideration and withdrawal of the rejection based on Lewis under 35 U.S.C. §102 (b) are respectfully requested.

***Liang***

Claims 1, 4, 9, 10 and 16 stood rejected under 35 U.S.C. §102 (a) as being anticipated by Liang et al., 2002, *Nutrition and Cancer*, Vol. 42(2): 217-223 (“Liang”). Applicants respectfully traverse this rejection.

Claims 1, 4 and 9 are directed to a benzotropolone derivative represented by a formula having specific R<sub>1</sub> R<sub>2</sub> and R<sub>3</sub> groups. Claims 10 and 16 are method claims requiring the use of a benzotropolone derivative.

Liang discloses inhibitory effects of black tea polyphenols (theaflavin, a mixture of theaflavin-3-gallate, theaflavin-3'-gallate, and theaflavin-3, 3'-digallate) on TPA-induced edema. Liang does not disclose a benzotropolone derivative as defined by the Applicants.

Notwithstanding, Applicants respectfully submit that in light of the Rule 131 declaration submitted herewith, the Liang reference has been removed as a prior art reference. Accordingly, the anticipation rejection based on Liang must be withdrawn.

#### ***IV. Response to Rejections Under 35 U.S.C. §103***

##### ***Lewis***

Claim 2 stood rejected under 35 U.S.C. §103(a) as obvious over Lewis et al., 1998, *Phytochemistry*, Vol. 49: 2511-2519. Applicants respectfully traverse this rejection.

Claim 2 is directed to a benzotropolone derivative, wherein the derivative is neotheaflavate B or its salt or ester compound.

Lewis teaches theaflavate B. The Examiner finds that the claimed neotheaflavate B is a stereoisomer of the compound taught by Lewis. The Examiner then concludes that the “instant compound is rendered obvious since a person of ordinary skill would reasonably expect the stereoisomers to exhibit the same characteristics absent a showing or teaching of the contrary.”

The Examiner appears to have relied on a *per se* rule that a stereoisomer is obvious in view of a disclosure of another stereoisomer in the prior art. Such reliance on “*per se* rules of obviousness,” however, is legally incorrect. *In re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995). To establish a *prima facie* case of obviousness, the Examiner must provide an explanation supported by evidence why the difference would have been obvious to one of ordinary skill in the art.

Although theaflavate and neotheaflavate have the same molecular formula, they are epimers and they are totally different compounds. Applicants respectfully submit that the claimed neotheaflavate B would not have been obvious to one of ordinary skill in the art because: (i) the prior art does not teach neotheaflavate B, much less its specific pharmacological activity discovered by the Applicants; (ii) the claimed neotheaflavate B is made by a process in which the starting compounds are catechin (C) and epicatechin gallate (ECG) whereas theaflavate B is made by the starting compounds epicatechin (EC) and ECG (see, for example, specification page 22 and Lewis at page 2518, left column, 2<sup>nd</sup> full paragraph under the subheading “*Synthesis of novel theaflavins/theaflavates*”); (iii) the pharmacological activity of a new stereoisomeric form cannot necessarily be envisaged in light of a known stereoisomeric form; (iv) there is no evidence that the prior art theaflavate B and the Applicants’ novel compound have common pharmacological properties or that an ordinary chemist in the field of theoflavins would have expected that the stereoisomer of theaflavate B would have antiinflammatory

activity, as disclosed by the Applicants, or that the stereoisomer would have any particular pharmacological property; (v) the Examiner has not shown that theaflavate B provides any suggestion to make or use the claimed neotheaflavate B; and (vi) the Examiner has not established any basis for concluding that one of ordinary skill in the art would have had a reasonable expectation that the claimed compounds would have similar biological properties as the compound taught by Lewis.

Accordingly, a *prima facie* case of obviousness based on the Lewis reference has not been established, and unless the Examiner has explanation supported by evidence showing that the differences between theaflavate B of Lewis and the claimed neotheaflavate B would have been obvious to one of ordinary skill in the art, this rejection must be withdrawn.

#### ***Liang***

Claims 11-20 stood rejected under 35 U.S.C. §103(a) as being obvious over Liang et al., 2002, Nutrition and Cancer, Vol. 42(2): 217-223. Applicants respectfully traverse this rejection.

Claims 11-20 are directed to a method for treating an inflammatory condition by using a composition having a benzotropolone derivative.

Liang is discussed above. Liang discloses anti-inflammatory activity of black tea polyphenols (theaflavin, a mixture of theaflavin-3-gallate, theaflavin-3'-gallate, and theaflavin-3, 3'-digallate). Liang does not teach or suggest anything about compositions containing benzotropolone derivatives and their anti-inflammatory activity.

Notwithstanding, Applicants respectfully submit that in light of the Rule 131 declaration submitted herewith, the Liang reference has been removed as a prior art reference. Accordingly, the obviousness rejection based on Liang must be withdrawn.

#### ***Wiseman***

Claims 21-23, 25 and 26 stood rejected under 35 U.S.C. §103(a) as being obvious over Wiseman et al., 1997, Critical Reviews in Food Science and Nutrition, Vol. 37(8):705-718 ("Wiseman").

Claims 21-23, 25 and 26 are directed to a method for neutralizing free radicals in a

patient by using a composition having a benzotropolone derivative.

Wiseman has been cited for disclosing a method for neutralizing reactive oxygen species and free radicals in a patient using tea antioxidants. Without conceding the validity of the rejection and solely to expedite the prosecution of this application, Applicants have elected to amend claim 21. Wiseman does not teach or suggest the claimed method using a benzotropolone derivative. Accordingly, this rejection must be withdrawn.

***Sang and Goodsall***

Claims 29-44 stood rejected under 35 U.S.C. §103(a) as being obvious over Sang et al., 2002, Tetrahedron Letters, Vol. 43: 7129-7133 (“Sang”) in view of Goodsall et al., U.S. Patent No. 6,113,965 (“Goodsall”).

In response, Applicants respectfully submit that, in light of the Rule 132 declaration submitted herewith, the Sang reference has been removed as a prior art reference thereby making this rejection moot. Reconsideration and withdrawal of the rejection are respectfully requested.

***V. Claim Objections***

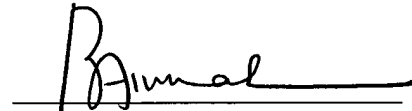
Claims 3, 5-8 and 24 were objected to as being dependent upon a rejected base claim. Applicants gratefully acknowledge the Examiner’s notation on page 8 of the Office that “[c]laims 3, 5-8 and 24 . . . . would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.” Applicants respectfully believe that the above amendments and discussion overcome the claim objections and place all the pending claims in condition for allowance.

***VI. Conclusion***

Applicants believe this response to be a full and complete response to the Office Action. Accordingly, favorable reconsideration in view of this response and allowance of all of the pending claims are earnestly solicited.

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Respectfully submitted,



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